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PATENT
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AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph at page 8, line 24 to page 9, line 8, with the following paragraph:

In another embodiment of the methods, the highly phosphorylated mannopyranosyl oligosaccharide compound comprises a compound having the formula $(6\text{-}P\text{-}M_x)_mL_n\text{-}R$ wherein:

M is a mannose or mannopyranosyl group;

L is a mannose or other hexose or other chemical groups;

P is a phosphate group linked to the C-6 position of M;

R comprises a chemical group containing at least one carbonyl-reactive group;

m is an integer from 2-3;

n is an integer from 1-15, wherein if n>1, M_n L_n are linked to one another by alpha (1,2), alpha (1,3), alpha (1,4), or alpha (1,6); and

x is an integer from 1-15. Thus, the highly phosphorylated mannopyranosyl oligosaccharide compound includes biantennary mannopyranosyl oligosaccharide compounds containing bis-M6P and triantennary mannopyranosyl oligosaccharide compounds containing bis-M6P or tri-M6P.

Please replace the paragraph at page 9, lines 14-17, with the following paragraph:

In another embodiment of the methods, the chemical compound containing carbonyl-reactive group includes any compound that reacts with carbonyl groups to form a hydrazone bond. Such compounds include hydrazines, hydrazides, ~~aminooxyls~~ aminooxy, and ~~semicarbozides~~ semicarbazides and the like.

Please replace the paragraph at page 12, lines 20-22, with the following paragraph:

The chemical compound containing the carbonyl-reactive group is any compound that reacts with carbonyl groups to form a hydrazone bond. Suitable such compounds include, for example, hydrazine, hydrazide, ~~aminooxyl~~ aminooxy, and ~~semicarbazide~~ semicarbazide and the like.

Please replace the paragraph at page 13, lines 6-15, with the following paragraph:

In an exemplary embodiment, the oligosaccharides are those bianternary and trianternary oligosaccharides that have the formula of $(6\text{-}P\text{-}M_x)_mL_n\text{-}R$ wherein:

M is a mannose or mannopyranosyl group;

L is a mannose or other hexose or other chemical groups;

P is a phosphate group linked to the C-6 position of M;

R comprises a chemical group containing at least one carbonyl-reactive group;

m is an integer from 2-3;

n is an integer from 1-15, wherein if n>1, ~~M_n~~ L_n are linked to one another by alpha (1,2), alpha (1,3), alpha (1,4), or alpha (1,6); and

x is an integer from 1-15.

Please replace the paragraph at page 14, line 7 to page 15, line 2, with the following paragraph:

Figure 1 is a schematic representation of the conjugation methods. In a first step, the reducing terminal sugar of oligosaccharides is derivatized to glycosylhydrazine (as shown) or other carbonyl-reactive groups (such as hydrazide, ~~semicarbozide~~ semicarbazide, ~~aminooxyl~~ aminooxy, etc). Such oligosaccharides must have one or more phosphate groups attached to the C 6' position(s) on mannopyranosyl groups (M6P). The oligosaccharide derivatives then react with the carbonyl (aldehyde) groups generated in the oxidized carbohydrates on glycoproteins to form covalent bond conjugates. The glycoproteins are oxidized according to at least three possible methods. By a first method, sialic acids on glycans are oxidized with a low concentration of sodium periodate (less than or equal to 10 mM) to generate the required carbonyl groups. A second method is suitable when terminal galactoses exist on the glycans, in which enzymatic oxidation is used. More specifically, galactose oxidase is used to oxidize the C 6' hydroxyl group on the galactose groups. This second oxidation method should not inactivate the glycoprotein. In an alternative embodiment of the second oxidation method, sialic acid groups on glycoprotein carbohydrates are removed using neuraminidase to expose the terminal galactoses, and then galactose oxidase is used to oxidize the terminal exposed galactoses as described for the first embodiment of the second oxidation method. By a third oxidation method, the hexoses on the glycans are oxidized with relatively high concentrations of sodium periodate, i.e. with sodium periodate having a concentration of greater than

about 10 mM and less than about 500 mM, to open the vicinal hydroxyl groups of the sugar ring. This third oxidation method is potentially harmful to certain glycoproteins that are sensitive to oxidation. To protect the glycoproteins from oxidation of amino acids, reductive agents such as beta-mercaptoethanol or cysteine or others are added to the oxidation reaction.

Please replace the paragraph at page 15, lines 18-28, with the following paragraph:

While the examples are done with the natural product of phosphopentamannose derivatized with hydrazine, it will be clear to one skilled in the art that various changes in form and detail can be made without departing from the true scope of the invention. For example, the oligosaccharide compounds useful in the present invention include any oligosaccharides that can be synthesized and derivatized with any chemical group, such as hydrazine, hydrazides, ~~semicarbozide~~ semicarbazide, ~~aminooxyl~~ aminooxy (L. A. Vilaseca et al., 4(6) BIOCONJUG. CHEM. 515 (1993)) groups, etc., that can react with carbonyl groups. Total synthesis of various mannopyranosyl oligosaccharides containing M6P has been reported (O. P. Srivastava and O. Hindsgaul, 155 CARBOHYDR. RES. 57 (1986); O. P. Srivastava and O. Hindsgaul, 52 J. ORG. CHEM. 2869 (1987); O. P. Srivastava and O. Hindsgaul, 161 CARBOHYDR. RES. 195 (1987)).